

KIDNEY DISEASE TARGETS AND USES THEREOF

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] This application is a continuation application of U.S. non-provisional application Ser. No. 16/210,539, filed Dec. 12, 2018, which is a continuation application of U.S. non-provisional application Ser. No. 15/132,462, filed Apr. 19, 2016, which is a divisional application of U.S. non-provisional application Ser. No. 14/173,082, filed Feb. 5, 2014, which is a continuation application of U.S. non-provisional application Ser. No. 13/183,696, filed Jul. 15, 2011, which is a divisional application of U.S. non-provisional application Ser. No. 12/557,303, filed Sep. 10, 2009 (issued as U.S. Pat. No. 7,998,689 on Aug. 16, 2011), which is a divisional application of U.S. non-provisional application Ser. No. 11/878,050, filed Jul. 20, 2007 (issued as U.S. Pat. No. 7,608,413 on Oct. 27, 2009), the contents each of which are hereby incorporated by reference in their entirety into this application.

FIELD OF THE INVENTION

[0002] This invention relates to the fields of molecular biology and oncology. Specifically, the invention provides a molecular marker and a therapeutic agent for use in the diagnosis and treatment of kidney diseases.

BACKGROUND OF THE INVENTION

[0003] The American Cancer Society estimates that there will be about 36,160 new cases of kidney cancer (22,490 in men and 13,670 in women) in the United States in the year 2005, and about 12,660 people (8,020 men and 4,640 women) will die from this disease. Kidney cancer (also referred to as renal cancer or renal cell carcinoma) mostly affects adults between 50 and 70 years of age. If detected early, kidney cancer is curable. However, symptoms may not appear until the tumor has grown to a large size or metastasized to other organs, at which point treatment is difficult.

[0004] The 5-year survival rate for individuals diagnosed with kidney cancer is about 90% for those individuals whose tumor is confined to the kidney, about 60% if it has only spread to nearby tissues, and about 9% if it has spread to distant sites (American Cancer Society, *Detailed Guide: Kidney Cancer*. “What Are the Key Statistics for Kidney Cancer (Renal Cell Carcinoma)?”).

[0005] The majority of kidney cancers are renal cell carcinomas (which accounts for over 90% of malignant kidney tumors), also known as renal adenocarcinomas or clear cell carcinomas. There are five main types of renal cell carcinoma that are identified based on microscopic examination of cell type: clear cell, papillary, chromophobe, collecting duct, and “unclassified.” Kidney cancers are also usually graded on a scale of 1 through 4 to indicate how similar the nuclei of the cancer cells are to the nuclei of normal kidney cells (grade 1 renal cell cancers have cell nuclei that differ very little from normal kidney cell nuclei and generally have a good prognosis, whereas grade 4 renal cell cancer nuclei look considerably different from normal kidney cell nuclei and have a worse prognosis). In addition to grade, kidney cancers are also characterized by stage, which describes the size of the cancer and degree of metastasis. The most commonly used staging system is that of the

American Joint Committee on Cancer (AJCC) (also referred to as the TNM system), although the Robson classification is an older system that may be occasionally used.

[0006] In addition to renal cell carcinomas, other types of kidney cancers include transitional cell carcinomas, Wilms tumors, and renal sarcomas. Wilms tumors are the most common type of kidney cancer in children and are extremely rare in adults. Benign (non-metastasizing) kidney tumors include renal cell adenomas, renal oncocytomas, and angiomyolipomas (American Cancer Society, *Detailed Guide: Kidney Cancer*. “What Is Kidney Cancer (Renal Cell Carcinoma)?”).

[0007] Risk factors for kidney cancer include the following: age older than 50 years; male (men are twice as likely to get kidney cancer compared to women); cigarette smoking; exposure to asbestos, cadmium, or organic solvents; obesity; a high-fat diet; and von Hippel-Lindau disease (a genetic condition that has a high incidence of kidney cancer).

[0008] Symptoms of kidney cancer include hematuria (blood in the urine), abdominal or low back pain, weight loss, fatigue, anemia, fever, high blood pressure, and leg or ankle swelling.

[0009] In addition to a detailed medical history, physical examination, and laboratory blood testing, diagnosis of kidney cancer may typically include a computed tomography (CT) scan, ultrasound, magnetic resonance imaging (MRI), intravenous pyelography (a kidney test that utilizes dye and x-rays), or arteriography (a test in which dye is applied to the blood vessels feeding the kidney). To detect metastatic disease, chest X-ray and bone scan may be implemented.

[0010] Treatment of kidney cancer in individuals whose tumor is confined to the kidney may involve surgical removal of the kidney (nephrectomy) and surrounding tissue. Radiation therapy may be applied to treat pain and advanced or metastatic kidney cancers or to help shrink a tumor that is causing obstruction. Immunotherapy, such as interferon and interleukin-2, may be used to boost the immune system in patients with advanced kidney cancer (*Journal of the American Medical Association*, JAMA Patient Page: Kidney Cancer).

[0011] One promising method for early diagnosis of various forms of cancer is the identification of specific biochemical moieties, termed “targets”, expressed differentially in the cancerous cells. The targets are either cell surface proteins, secreted proteins, or cytosolic proteins. Antibodies which will specifically recognize and bind to the targets in the cancerous cells potentially provide powerful tools for the diagnosis and treatment of the particular malignancy.

SUMMARY OF THE INVENTION

[0012] The present invention is based on the identification of certain cell surface proteins, secreted proteins, and/or cytosolic proteins that are differentially expressed in kidney disease. A malignant cell often differs from a normal cell by a differential expression of one or more proteins. These differentially expressed proteins, and the fragments thereof, are important markers for the diagnosis of kidney disease. The differentially expressed proteins of the present invention and the nucleic acids encoding said proteins and the frag-